-continued

<213> ORGANISM: primer

<400> SEQUENCE: 6

gaaaccagct tcaaggcact g 21

<210> SEQ ID NO 7
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: primer

<400> SEQUENCE: 7

attcagtgcc atgggacata g 21

What is claimed is:

1. A method comprising:

a) providing a reaction mixture comprising a single stranded nucleic acid template, a primer having at least 15 bases which is complementary to a portion of the single stranded nucleic acid template and a plurality of oligonucleotide 5'-monophosphates wherein each oligonucleotide 5'-monophosphate consists of not more than 10 bases and wherein each of the oligonucleotide 5'-monophosphates is labeled;

b) hybridizing the primer with the template under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to form a primer-template hybrid having a single stranded region and a double stranded region;

c) ligating more than one of the plurality of labeled oligonucleotide 5'-monophosphates in a contiguous manner onto the primer in one continuous process under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to extend the double stranded region and synthesize a labeled complementary nucleic acid strand, wherein ligation of oligonucleotide 5'-monophosphates only occurs in the presence of the hybridized primer.

2. The method of claim 1 wherein each of the plurality of oligonucleotide 5'-monophosphates consists of 5 bases.

3. The method of claim 1 wherein each of the plurality of oligonucleotide 5'-monophosphates is of identical length.

4. The method of claim 1 wherein some of the plurality of oligonucleotide 5'-monophosphates contain a different number of bases from other of the plurality of oligonucleotide 5'-monophosphates.

5. The method of claim 1 wherein the ligation is performed by means of a ligase enzyme.

6. The method of claim 5 wherein the ligase enzyme is selected from T4 ligase, T7 ligase, Tth ligase, Taq ligase and *E. coli* DNA ligase.

7. The method of claim 5 wherein the ligase enzyme is T4 DNA ligase.

8. The method of claim 1 wherein the primer is immobilized onto a solid phase.

9. The method of claim 1 wherein the primer is in a solution.

10. The method of claim 1 further comprising separating the labeled complementary nucleic acid strand from the template.

11. The method of claim 1 wherein each labeled oligonucleotide 5'-monophosphate is labeled with the same label.

12. The method of claim 1 wherein each oligonucleotide 5'-monophosphate is labeled with a label that is specific for and identifies that oligonucleotide 5'-monophosphate.

13. The method of claim 1 wherein each oligonucleotide 5'-monophosphate contains 1 label.

14. The method of claim 1 wherein each label is a detectable label selected from radioisotopes, chemiluminescent labels, fluorescent labels, colorimetric labels and enzymes.

15. The method of claim 1 wherein each label is selected from binding proteins, antigens, antibodies, haptens and oligonucleotides.

16. The method of claim 1 further comprising the incorporation of at least one nonextendable oligomer the ligation of which terminates synthesis of the nucleic acid strand.

17. The method of claim 16 wherein each of the nonextendable oligomers is selected from oligomers which have a dideoxy base at the 3'-end, oligomers which have a blocked 3'-OH group at the 3'-end and oligomers which lack a phosphate group at the 5'-end.

18. The method of claim 1 wherein the synthesis of the labeled complementary nucleic acid strand synthesized in step c) is terminated at a predetermined position by excluding from the plurality of oligonucleotide 5'-monophosphates at least one oligonucleotide 5'-monophosphate which is complementary to the single stranded nucleic acid template and has a sequence necessary to extend the double stranded region.

19. The method of claim 1 wherein the synthesis of the strand of nucleic acid is unidirectional and proceeds by ligation to the 3' end of the primer.

20. The method of claim 1 wherein the primer contains a 5'-phosphate group and the synthesis of the strand of nucleic acid is unidirectional and proceeds by ligation to the 5' end of the primer.

21. The method of claim 1 wherein the primer contains a 5'-phosphate group and the synthesis of the strand of nucleic acid proceeds from both ends of the primer.

22. The method of claim 1 wherein the single stranded nucleic acid template has a segment of known sequence, wherein the primer is complementary to a portion of the segment of known sequence and wherein the plurality of labeled oligonucleotide 5'-monophosphates comprises a set of labeled oligonucleotide 5'-monophosphates selected to be complementary to a part of the segment of known sequence of the template adjacent to the portion of the segment of known sequence to which the primer is complementary.

23. A method for synthesizing a labeled double stranded nucleic acid wherein both strands are labeled comprising:

a) providing a reaction mixture comprising a double stranded nucleic acid template, a first primer which is complementary to a region of a first strand of the template, a second primer which is complementary to a region of a second strand of the template, wherein both primers have at least 15 bases, and a plurality of labeled oligonucleotide 5'-monophosphates wherein each oligonucleotide 5'-monophosphate consists of not more than 10 bases and wherein each oligonucleotide 5'-monophosphate is labeled;

b) separating the first and second strands of the double stranded nucleic acid;

c) hybridizing the first and second primers with the separated strands under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to form first and second primer-template hybrids;

d) ligating more than one of the plurality of labeled oligonucleotide 5'-monophosphates in a contiguous manner onto each primer-template hybrid in one continuous process under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to extend the first and second primers thereby producing double stranded nucleic acid, wherein ligation of oligonucleotide 5'-monophosphates only occurs in the presence of the hybridized primer; and e) repeating steps b–d at least once, thereby synthesizing a labeled double stranded nucleic acid wherein both strands are labeled.

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